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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/672,725	09/28/2000	Penny J. Stocker	G0307/7017	7328

7590 12/12/2002

Wolf Greenfield & Sacks PC
600 Atlantic Avenue
Boston, MA 02210

EXAMINER	
RAO, MANJUNATH N	
ART UNIT	**PAPER NUMBER**
1652	14

DATE MAILED: 12/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/672,725	STOCKER ET AL.	
	Examin r	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,14-16,18-23,25,27,29,30,38 and 45* is/are pending in the application.

4a) Of the above claim(s) *14-16,23,25,27,29,30,38 and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5 and 18-22* is/are rejected.

7)☒ Claim(s) *2-4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4, 5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-5, 14-16, 18-23, 25, 27, 29-30, 38 and 45 are presently pending in this application. Claims 1-5 and 18-22 are now under consideration. Claims 14-16, 23, 25, 27, 29-30, 38 and 45 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-4 in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Claim Objections

Claim 18 is objected to because of the following informalities: Claim 18 depends from a non-elected claim 14. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18, 20 and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for DNA isolated from a dog, with SEQ ID NO:1 encoding a polypeptide with SEQ ID NO:2, does not reasonably provide enablement for any DNA from any source encoding P-glycoprotein including fragments, variants, mutants and recombinants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 18, 20 and 22 are so broad as to encompass any DNA isolated from any source capable of encoding P-glycoprotein polypeptide or fragment thereof , and vectors and host cells comprising such DNAs. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNA sequences that are broadly encompassed by the claims.

The applicants propose to use the above polynucleotides for a variety of processes such as recombinant protein preparation, as hybridization probes, for identification of mRNA of interest. Since the nucleotide sequence determines the type of protein and the ultimate function of the encoded protein and since only nucleic acids with very high percent homology can be used as a probe for either identifying mRNA or for screening a cDNA library, changing the nucleotide

sequences as proposed by the applicants and/or addition of substantial amount of additional nucleotide sequence unrelated to the nucleic acid sequence of SEQ ID NO:1 may not lead to desired function of the polynucleotides. This is because the changes suggested by the applicants will result in an enormous number of nucleotide sequences that will hybridize to several unrelated mRNAs instead of hybridizing specifically to mRNA of interest and similarly may hybridize to cDNAs totally unrelated to cDNA of interest while screening a cDNA library. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of a single P-glycoprotein from dog.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or modifications of nucleotides, as encompassed by the instant claims, and the base changes within a nucleic acid's sequence can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given DNA to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any DNA encoding a P-glycoprotein activity because the specification does not establish: (A) regions of the DNA sequence which may be modified without effecting the above mentioned activity/utility; (B) the general tolerance of P-glycoprotein encoding DNA sequence to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any P-glycoprotein encoding DNA with an expectation of obtaining the desired biological function and utility; and (D) the specification

provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including all or any DNA encoding P-glycoprotein or fragment thereof isolated from all or any source. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of DNAs having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 18, 20 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules encoding P-glycoprotein or fragment thereof.

The specification does not contain any disclosure of the structure of all DNA sequences that encode any P-glycoprotein or fragment thereof. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of having many different structures. Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species (SEQ ID NO:1) of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one

skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 5, 18-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1, 5 and 18 are directed to allelic variants of polynucleotides encoding the polypeptide with SEQ ID NO:2 or 23, 25, 27 comprising a genus of DNA molecules.

There is no specific definition in the specification for "allelic sequence". However in the art, allelic sequences are known as an alternative form of the gene (of the same species) which may result in at least one mutation in the nucleic acid sequence. Alleles may result in altered mRNAs or polypeptides whose structure or function may or may not be altered. This definition does not provide any specific information about the structure of naturally occurring (alleles) variants of polynucleotides encoding SEQ ID NO:2 or 23, 25, 27 (i.e. where are the regions within which mutations are likely to occur) nor discloses any function for naturally occurring variants. There is no description of the mutational sites that exist in nature, and there is no description of how the structure of the polynucleotides encoding SEQ ID NO:2 or 23, 25, 27 relates to the structure of any naturally occurring alleles. The general knowledge in the art concerning alleles dose not provide any indication of how one allele is representative of unknown alleles. The nature of alleles is such that they are variant structures, and in the present

state of the art, structure of one does not provide guidance to the structure of others. The genus of DNAs that comprise the above claimed DNA molecules is a large variable genus with different structures and potentiality of encoding many different proteins. Therefore, many structurally and functionally unrelated DNAs are encompassed within the scope of these claims. The specification discloses only three species of the claimed genus (i.e. the sequences encoding SEQ ID NO:2, 23, 25 and 27) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 18-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Steingold et al. (Anticancer Res., 1998, Vol. 18:393-400). This rejection is based upon the public availability of a printed publication. Claims 1, 5, 18-22 of the instant application are drawn to nucleic acid molecule isolated from dog, selected from the group consisting of a nucleic acid that encodes the

amino acid sequence SEQID NO:2, allelic variants of the same wherein the allelic variants exclude SEQ ID NO:3 or 5 and wherein the allelic variants encode the amino acid sequences SEQ ID NO:23, 25 or 27, a nucleic acid which encodes a P-glycoprotein or a fragment thereof, vectors and host cells comprising the same. Steingold et al. disclose a nucleic acid isolated from a dog tissue which encodes P-glycoprotein. Furthermore, while Examiner was unable to find a sequence match with SEQ ID NO:1 and the nucleotide sequence disclosed in the reference, Examiner takes the position that the polynucleotide disclosed in the reference is an allelic variants of SEQ ID NO:1 or a nucleic acid encoding either polypeptide SEQ ID NO:23, 25 or 27. The reference also discloses vectors and host cells expressing the polynucleotide (Invitrogen TA cloning system). Thus Steingold et al. anticipate claims 1, 5 and 18-22 of this application as written.

Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Conclusion

Claims 2-4 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 7:30 a.m. to 4:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Manjunath N. Rao Ph.D.
Patent Examiner
12/10/02